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SULPHATHIAZOLE IN THE TREATMENT OF GONORRHŒA

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THE toxic effects of sulphapyridine which may interfere seriously with precision work made an investigation of a less toxic remedy promising equal therapeutic potency desirable, and accordingly this investigation of sulphathiazole (Thiazamide or M. & B. 760) was carried out.

This preliminary report deals with a series of 55 male and 23 female cases of gonorrhœa treated by sulphathiazole. Though the series is small, an attempt has been made to follow the lines of a previous communication (*B.M.J.* 15-6-40). Reference to that article will elucidate any difficulty in the interpretation of terms used to designate cases.

Male Cases.—The two schemes of dosage used for male patients were as follows :—

SCHEME I				SCHEME II			
Day 1-3	.	.	6 tablets per day = 18	8 tablets per day = 24			
„ 4-6	.	.	4 „ „ „ = 12	6 „ „ „ = 18			
„ 7-9	.	.	2 „ „ „ = 6	4 „ „ „ = 12			
			Total . 36	Total . 54			

In Table I (on p. 245) the 55 male cases have been analysed in two groups according to the dosage of sulphathiazole.

Cases responding favourably (41).—The following clinical observations were made on the cases showing a favourable response :—

The average number of days before the urethral smear became free of gonococci was 2.3. The average number of days before the urine became clear was 5.0. Three of these cases were complicated by an epididymitis at the outset—one acute and two subacute. They were admitted to hospital. The epididymitis resolved rapidly and the patients were able to leave at the end of the nine days' course.

SULPHATHIAZOLE TREATMENT—GONORRHOEA

TABLE I

	SCHEME I (36 tabs. in 9 days)	SCHEME II (54 tabs. in 9 days)
Number of cases treated	35	20
Regarded as cured. { Discharged cured *	10	7
{ Ceased attending during observation period * but apparently cured	9	4
{ Transferred during observation period * but apparently cured	5	6
	24	17
Not regarded as cured. { Ceased attending or defaulted during chemotherapy	1	1
FAILURES	10 (28.5 per cent.)	2 (10 per cent.)

* The period of observation aimed at was 12 weeks after the completion of the course of chemotherapy.

One case of chronic prostatitis previously resistant to sulphapyridine and urethral irrigations cleared up following administration of 36 tablets of sulphathiazole without further local treatment. One case of uncomplicated posterior urethritis previously unaffected by sulphapyridine responded to 54 tablets of sulphathiazole.

Failures.—Interest is naturally focussed on those cases in which sulphathiazole did not effect a cure. The percentage of failures with the lower dosage was 28.5 and with the higher dosage 10. The failures occurring under each scheme will now be analysed :—

Cases receiving 36 tablets in 9 days.—Two relapsed quickly, with gonococci in the discharge, after alcohol. Two showed no sign of any improvement. Six had become drug resistant after having taken sulphapyridine in doses varying from 20 to 60 gms., and were not cured by the subsequent administration of sulphathiazole. Of these six, three patients improved on this drug, but, immediately the tablets were stopped, discharge, containing gonococci, returned. The remaining three patients showed no clinical or bacteriological improvement during the administration and thereafter developed complications, viz., folliculitis (two) and periurethral abscess (one).

Cases receiving 54 tablets in 9 days.—One patient

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showed a relapse following alcohol four days after the cessation of the tablets. His clinical and bacteriological response prior to this had been good. One patient, who had previously had 46 tablets of sulphapyridine, showed no response to sulphathiazole.

In so far as it is permissible to draw conclusions from this analysis, the following points may be adduced :—

An effective concentration of sulphathiazole must be attained by using adequate dosage. If an ineffective dosage is used, the gonococcus may become resistant to this drug or to other sulphonamides.

Like other sulphonamides, sulphathiazole may be unable to deal with the gonococcus when it has produced a closed pus pocket.

Alcohol acts effectively as a provocative in cases where the gonococci have not been completely killed, or alternatively, if taken concurrently, may determine failure of the drug.

Female Cases.—For the *uncomplicated* cases, two schemes of treatment were adopted, each comprising a total of 30 tablets. In the first scheme, six tablets per day were given for two days, then three tablets daily for six days, *i.e.*, 30 tablets in 8 days. In the second scheme, six tablets per day were given for five days, *i.e.*, 30 tablets in 5 days.

In Table II the 13 uncomplicated female cases are analysed in two groups according to the scheme of dosage :—

TABLE II

	SCHEME I (30 tabs. in 8 days)	SCHEME II (30 tabs. in 5 days)
Number of cases treated . . .	9	4
Discharged cured . . .	5 (average observation 8 months.)	1
Regarded as cured. { Transferred while under observation but apparently cured.	2 (observed 3 months.)	1 (observed 5 months.)
{ Still under observation but apparently cured.	2 (9 months' and 5 months' observation.)	2 (7 months' and 8 months' observation.)
FAILURES	Nil.	Nil.

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The *complicated* female cases were usually given larger dosage. They are analysed in Table III.

TABLE III

Case Number	Nature of Complication	Daily Dosage	Total Tablets	Result	Months of Observation
A. 6168 .	Arthritis. Pregnancy.	4 24D × 3* 6D × 4	4 72 24	Apparently cured.	6
A. 5717 .	Secondary syphilis. Bartholinian abscess. Alcoholism.	5D × 7	35	Apparently cured, but defaulted.	3
A. 5979 .	Secondary Syphilis. Genital warts. Prostitute.	3 6D × 2 5D × 5	3 12 25	Apparently cured.	1½
A. 6348 .	Mother of one of the cases of vulvo-vaginitis.	10D × 3 5D × 4 plus 12 later at M.P.	30 20	Apparently cured.	4
A. 6347 .	Late gonorrhœa. Acute salpingitis.	12D × 2 10D × 2 5D × 3	24 20 15	Apparently cured.	3
A. 6138 .	Late gonorrhœa. Intolerant of sulphapyridine.	4D × 5	19	Apparently cured.	5
A. 6253 .	Secondary syphilis. Albucid locally failed. Prostitute.	4D × 8	32	Great improvement	Defaulted.

* 24D × 3, etc., indicates 24 tablets per day for 3 days.

Vulvo-vaginitis.—Three cases were treated and the particulars are tabulated on p. 248.

The results obtained in the 23 female cases are summarized in the subjoined table :—

	Females
Number of cases	23
Regarded as cured	21
Defaulters, uncured	1
Failures	1

Toxic Effects.—All patients were instructed to drink plenty of water along with the tablets and throughout

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TABLE IV

Case Number	Nature of Case	Daily Dosage	Total Tablets	Result	Months of Observation
A. 6349	Severe, acute.	5D \times 6*	30	Apparently cured.	4
A. 6099	Severe, acute. Previous Sulphapyridine failure and rash.	5D \times 8	42	Apparently cured. Defaulted.	2
A. 6573	Severe, acute. Previous Sulphapyridine relapse and rash.	5D \times 2 3D \times 5	10 15	Improvement then relapse.	1

* *Q.v.* legend under Table III.

the course of treatment, and in no case was there ever any suspicion of hæmaturia or anuria.

Of the *male* patients, three out of the total of 55 complained of slight headache and one of nausea. No other toxic phenomena were observed. It was never necessary to modify the course of treatment.

Of the *female* patients, none of the *adults* showed any toxic manifestations.

Of the vulvo-vaginitis cases, one *child* of 6 years developed a slight rash which disappeared with continued treatment. She also had nausea with one tablet four-hourly, but this disappeared on reducing the dose to a half tablet four-hourly (three tablets in the 24 hours).

CONCLUSIONS

This small series of cases affords corroboration for the claims already made that sulphathiazole is an effective drug in the treatment of gonorrhœa, that its efficacy is comparable to that of sulphapyridine, and that its toxic effects are much slighter than those of sulphapyridine. In particular, mental depression was not complained of by any patient.

The eligibility of sulphathiazole for the position of first choice in the treatment of gonorrhœa is a question of much importance to the manufacturers as well as to clinicians. If the conclusions above stated are substantiated, the organization of productive capacity towards increased output of sulphathiazole will be stimulated and increased supplies will be welcomed by clinicians.

VENEREAL DISEASES IN ENGLAND AND WALES

SUMMARY

The therapeutic action of sulphathiazole has been studied in 55 male and 23 female cases of gonorrhœa.

Some possible causes of failure of the drug are discussed.

For supplies of Thiazamide the authors are indebted to Pharmaceutical Specialities (May & Baker) Ltd., Dagenham.

VII

THE PRESENT TREND OF INCIDENCE OF VENEREAL DISEASES IN ENGLAND AND WALES, AND METHODS OF CONTROL *

By L. W. HARRISON, D.S.O., F.R.C.P.

As a preliminary to a discussion on the present trend of incidence of V.D. in this country, it seems appropriate that something should be said about the position we had reached in this respect by the year 1939, because it probably has a bearing on the fact that since the outbreak of the war venereal diseases have not increased in this country to anything like the extent which we feared.

I am inclined to think that the title of this discussion should be the present trend of incidence of syphilis because we are very much in the dark as regards the incidence of gonorrhœa in the civilian population and have no reliable comparative statistics. Our Service colleagues will no doubt, however, give us some idea of the relative incidence of gonorrhœa in the Forces and from this and our knowledge of the incidence of syphilis we may be able to form some idea of the position in respect of gonorrhœa in civilians.

As regards syphilis, prior to the war we had good reason for believing that the great majority of the early infections in civilians coming under medical care in this country were being dealt with in the treatment centres. Sometimes in the past it has been suggested that many

* An address delivered to the Medical Society for the Study of Venereal Diseases on July 26th, 1941.